

This listing of claims will replace all prior versions, and listings, of claims in this application.

Listing of the claims:

---

Claim 1 (previously cancelled).

2. (Currently Amended) A polynucleotide comprising a modified Cre recombinase gene comprising SEQ ID NO:1 ~~which is modified such that it is expressed in elevated levels compared to the unmodified Cre recombinase gene;~~ and an inducible promoter operatively linked to the modified Cre recombinase gene.

3. (Previously Amended) The polynucleotide according to claim 2, further comprising at least one of a marker gene, a nucleic acid encoding a nuclear transport signal, and a Kozak sequence.

Claim 4 (previously cancelled).

5. (Currently Amended) The polynucleotide according to claim 2, wherein the inducible promoter is a ~~location-specific~~ thymidine kinase promoter.

6. (Cancelled).

7. (Previously Amended) A polynucleotide complementary to the polynucleotide according to Claim 2.

8. (Currently Amended) A non-human animal into which ~~the gene encoding the~~ polynucleotide according to Claim 2 is introduced, wherein an active Cre recombinase is expressed in the animal.

9. (Currently Amended) An organ into which ~~the gene encoding the~~ polynucleotide according to Claim 2 is introduced, wherein an active Cre recombinase is expressed in the organ.

10. (Currently Amended) A tissue into which ~~the gene encoding~~ the polynucleotide according to Claim 2 is introduced, wherein an active Cre recombinase is expressed in the tissue.

11. (Twice Amended) A cell into which ~~the gene encoding~~ the polynucleotide according to Claim 2 is introduced, wherein an active Cre recombinase is expressed in the cell.

12. (Currently Amended) A method of knocking-in a desired gene ~~in a location controlled and/or time-controlled manner~~; comprising the steps of:

(1) introducing a first gene construct and a second construct into cells, tissues, organs or whole bodies,

wherein the first gene comprises a polynucleotide according to Claim 2; and the second gene construct comprises a first loxP sequence, a second loxP sequence located downstream of the first loxP sequence, a second promoter sequence located upstream of the first loxP sequence, and the desired gene located downstream of the second loxP sequence,

(2) expressing a Cre recombinase gene by the inducible promoter ~~in a location-controlled and/or time-controlled manner~~, and

(3) placing the desired gene under control of the promoter sequence in the second gene construct by site specific recombination on the second gene construct by Cre recombinase expressed in step (2), thereby knocking-in the desired gene ~~in a location-controlled manner and/or time-controlled manner~~.

13. (Currently Amended) A method of knocking-out a desired gene ~~in a location controlled and/or time-specific manner~~; comprising the steps of:

(1) introducing a first gene construct and a second gene construct into cells tissues organs or whole bodies,

wherein the first gene construct comprises a polynucleotide according to Claim 2; and the second gene construct comprises a first loxP sequence, a second loxP sequence located downstream of the first loxP sequence, a promoter sequence located upstream or downstream of the first loxP sequence, and the desired gene located downstream of the promoter and the first loxP sequence,

(2) expressing a Cre recombinase gene by the inducible promoter ~~in a location-controlled manner~~, and

(3) inserting a part or whole of the desired gene from the second gene construct by site specific recombination with the second gene construct mediated by Cre recombinase expressed in step (2), thereby knocking-out at least a part or whole of the desired gene, ~~in a location-controlled and/or time-controlled manner~~.

14. (Previously Amended) The method of claim 12, wherein the desired gene is selected from the group consisting of a xenograft antigen, carcinogenic antigen, and anti antibody-production-associated-molecule antibody.

15. (Currently Amended) A transgenic animal into which a desired gene is knocked-in ~~in a location-controlled and/or time-controlled manner in accordance with~~ according to the method of claim 12.

16. (Currently Amended) A transgenic animal from which a second desired gene is knocked-out ~~in a location-controlled and time-controlled manner in accordance with~~ according to the method of claim 13.

17. (original) The transgenic animal according to claim 16, wherein the animal is swine.

18. (Previously Amended) An organ from the transgenic animal according to claim 16.

19. (Previously Amended) A tissue from the transgenic animal according to claim 16.

20. (Previously Amended) A cell from the transgenic animal according to claim 16.

21. (Previously Amended) A method for treating a disease caused by malfunction of an organ, comprising a step of transplanting the organ according to Claim 18, into an organism.

23. (Previously Amended) A method for treating a disease caused by malfunction of a tissue, comprising a step of transplanting the tissue according to Claim 19 into an organism.

24. (Previously Amended) A method for treating a disease caused by malfunction of a cell, comprising a step of transplanting the cell according to Claim 20 into an organism.

Claims 25-35 (Cancelled).

36. (New) The method of claim 13, wherein the desired gene is selected from the group consisting of a xenograft antigen, carcinogenic antigen, and anti antibody-production-associated-molecule antibody.

---